

**CLAIMS:**

1-63 (Cancelled).

65. (New) An apparatus for exciting biosensor fluorescence, said apparatus comprises:

- (a) a light source which generates and transmits a certain light signal;
- (b) annularizing means by which a substantially uniformly distributed and cylindrical beam of light containing an initial first amount of light power and which is impinging upon said annularizing means becomes topologically transformed with minimal loss of said initial first amount of light power into an emergent second beam which is substantially uniformly distributed in power within an annular shell or region on the outside of the beam, the inside region being substantially devoid of light power;
- (c) an optical fiber waveguide which receives said transmitted light signal in which an evanescent field is generated and having a plurality of a certain molecule of a first type affixed to its surface; and
- (d) processing means, connected to said light source and to said waveguide for using said evanescent field to excite biosensor fluorescence.

66. (New) A method to be used with apparatus of claim 65, said method providing measurement of binding affinity between a plurality of the first type of molecule and a plurality of a certain second type of molecule, said method comprising the following steps in combination:

- (a) providing an evanescent sensor apparatus having an optical waveguide and a light source adapted to generate and transmit light to said optical waveguide and a means to collect light from said optical waveguide;
- (b) said optical waveguide having a plurality of the molecules of the first type affixed to its surface;
- (c) providing at least one certain concentration of molecules of the second type, said molecules being tagged with molecules of a chemical belonging to that

class of chemicals which, when bound to said optical waveguide, produces an alteration in a certain characteristic of light collected from said waveguide;

(d) providing means by which the surface of said optical waveguide is brought into contact with test solutions;

(e) providing means for acquiring paired measurements of time and response to light collected from said evanescent sensor, said time measurements having an interval between them which is at most on the order of seconds;

(f) bringing one of said concentrations of tagged molecules into contact with said evanescent sensor for a certain period of time while acquiring said paired measurements;

(g) removing said concentration of tagged molecules from contact with said evanescent sensor and bringing into contact with said sensor, a solution containing no molecules of said second type, and maintaining contact for a certain time while acquiring additional paired measurements of time and response to light collected from said evanescent sensor; and

(h) computing said binding affinity between said first type of molecule and said second type of molecule using data from said paired measurements to provide initial rate of binding and initial rate of unbinding for solution of equations relating these rates to binding affinity.

67. (New) A method to be used with apparatus of claim 65, said method providing measurement of the relative binding activity of a sample, said method comprising in combination:

(a) providing an evanescent sensor having an optical waveguide and a light source adapted to generate and transmit light to said optical waveguide and collect light from said optical waveguide;

(b) said optical waveguide having a plurality of the molecules of the first type affixed to its surface;

(c) providing at least one sample solution containing molecules of a second type, said molecules being tagged with molecules belonging to that class of chemicals which interact with light from said light source in a manner so as to alter a

characteristic of light collected after passing through said molecule tags and said sample being created in a diluent which preserves the binding characteristics of said molecules of said first and second types;

(d) creating a calibration standard comprising certain concentration of tagged molecules of a second type, said molecules being from a source having a certain known binding activity with respect to said molecules of a first type;

(e) providing means by which the surface of said optical waveguide is brought into contact with test solutions;

(f) providing means for acquiring paired measurements of time and response to light collected from said evanescent sensor, said time measurements having an interval between them which is at most on the order of seconds;

(g) bringing said calibration standard into contact with said evanescent sensor for a certain period of time while acquiring said paired measurements;

(h) removing said calibration standard from contact with said evanescent sensor and bringing into contact with said sensor, said sample solution for a certain period of time while acquiring said paired measurements; and

(i) creating a ratio between the sensor response to the sample (S) and sensor response to the calibrator (C), said ratio being obtained by any method providing a comparison of the two responses, comparing said ratio for subsequent samples utilizing identical calibration standards to provide relative binding activities between said samples.

68. (New) A method to be used with apparatus of claim 65, said method providing measurement of the effective binding affinities between a plurality of the first type of molecule and a plurality of a certain second type of molecule when said molecules exhibit co-operative binding behaviour, said method comprising in combination:

(a) providing evanescent sensors having an optical waveguide and a light source adapted to generate and transmit light to said optical waveguide and collect light from said optical waveguide;

(b) said optical waveguide having a plurality of the molecules of the first type affixed to its surface;

(c) providing a solution containing certain molecules of said second type, said molecules being tagged with molecules belonging to that class of chemicals which interact with light from said light source in a manner so as to alter a characteristic of light collected after passing through said molecular tags;

(d) creating a calibration standard comprising a certain concentration of said tagged molecules of a second type;

(e) creating several dilutions of a standard sample, said standard sample dilutions comprising molecules having a certain known binding affinity with respect to molecules of said second type, said dilutions also containing a certain concentration of said tagged molecules of said second type;

(f) creating several dilutions of a test sample, said test sample dilutions comprising molecules having with respect to molecules of said second type, a binding affinity which is to be measured, said dilutions also containing a certain concentration of said tagged molecules of said second type, said certain concentration being identical to that used to create standard sample dilutions;

(g) providing means by which the surface of each of said optical waveguides is brought into contact with solutions; and

(h) providing means for acquiring paired measurements of time and response to light collected from said evanescent sensor, said time measurements having an interval between them which is at most on the order of seconds;

(i) bringing said calibration standard into contact with a first evanescent sensor for a certain period of time while acquiring said paired measurements;

(j) removing said calibration standard from contact with said first evanescent sensor and bringing into contact with said sensor, said one dilution of a sample solution for a certain period of time while acquiring said paired measurements;

(k) creating a ratio between the sensor response to the sample (S) and sensor response to the calibrator (C), said ratio being obtained by any method

providing a comparison of the two responses regardless of the mathematical form of the sensorgram.

(l) repeating steps (i), (j) and (k) for each test sample dilution and each standard dilution;

(m) identifying from said ratios obtained on said standard sample solutions, that concentration for which the ratio is the highest;

(n) identifying from said ratio obtained on said test sample solutions, that concentration for which the ratio is the highest; and

(o) computing the effective binding affinity of said test sample for said molecules of the second type from known relationship between the ratio and the binding affinity and concentrations of test and standard solutions.

69. (New) The method according to claim 66, wherein the concentration of the molecule of the second type is measured in solution.

70. (New) The method according to claim 66, wherein the first type of molecule is a receptor and the second type of molecule is a response element, and wherein a pharmacological agent is used to affect the binding between the first and second molecules.